

# **EXHIBIT B**

Please type a plus (+) inside this box +

PTO/SB/05 (03-01)

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<b>UTILITY PATENT APPLICATION TRANSMITTAL</b> <i>(Only for new nonprovisional applications under 37 CFR 1.53(b))</i>	Attorney Docket No.	S93-160 CON2	Total Pages	77
	First Named Inventor or Application Identifier			
	Cohen			
	Express Mail Label No.	EV 159 436 544 US		

<b>APPLICATION ELEMENTS</b> <i>See MPEP chapters 600 concerning utility patent application contents.</i>	<b>Address to:</b> <b>Commissioner for Patents</b> <b>P.O. Box 1450</b> <b>Mail Stop PATENT APPLICATION</b> <b>Alexandria, VA 22313-1450</b>
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<p>1. <input checked="" type="checkbox"/> Fee Transmittal Form [Total Pages 4] <i>(Submit an original, and a duplicate for fee processing)</i></p> <p>2. <input checked="" type="checkbox"/> Applicant claims Small Entity status, see 37 C.F.R. § 1.27</p> <p>3. <input checked="" type="checkbox"/> Specification [Total Pages 47] <i>(preferred arrangement set forth below, MPEP 1503.01)</i> - Descriptive title of the Invention - Cross Reference to Related Applications - Statement Regarding Fed sponsored R&amp;D - Reference to Microfiche Appendix - Background of the Invention - Brief Summary of the Invention - Brief Description of the Drawings (if filed) - Detailed Description of the Invention (including drawings, if filed) - Claim(s) - Abstract of the Disclosure</p> <p>4. <input checked="" type="checkbox"/> Drawing(s) (35 USC 113) [Total Sheets 1]</p> <p>5. <input checked="" type="checkbox"/> Oath or Declaration [Total Sheets 4] a. <input type="checkbox"/> Newly executed (original or copy) b. <input checked="" type="checkbox"/> Copy from a prior application (37 CFR 1.63(d)) <i>(for continuation/divisional with Box 18 completed)</i> i. <input type="checkbox"/> DELETION OF INVENTOR(S) Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b).</p> <p>6. <input checked="" type="checkbox"/> Application Data Sheet. See 37 CFR 1.76 [Total Sheets 2]</p>	<p>7. <input type="checkbox"/> CD-ROM or CD-R in duplicate, large table or Computer Program (Appendix)</p> <p>8. <input checked="" type="checkbox"/> Nucleotide and/or Amino Acid Sequence Submission a. <input type="checkbox"/> Computer Readable Form (CRF) b. <input type="checkbox"/> Specification Sequence Listing on: i. <input type="checkbox"/> CD-ROM or CD-R (2 copies); or ii. <input checked="" type="checkbox"/> paper [Total pages 11] c. <input type="checkbox"/> Statement verifying identity of above copies</p>
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<b>ACCOMPANYING APPLICATION PARTS</b>	
9. <input type="checkbox"/> Assignment Papers (cover sheet & document(s)) 10. <input checked="" type="checkbox"/> Power of Attorney and Transmittal (copy from prior application) 11. <input type="checkbox"/> English Translation Document (if applicable) 12. <input type="checkbox"/> Information Disclosure Statement (IDS)/PTO-1449 <input type="checkbox"/> Copies of IDS Citations 13. <input checked="" type="checkbox"/> Preliminary Amendment [Total Sheets 5] 14. <input checked="" type="checkbox"/> Return Receipt Postcard (MPEP 503) <i>(Should be specifically itemized)</i> 15. <input type="checkbox"/> Certified Copy of Priority Document(s) <i>(if foreign priority is claimed)</i> 16. <input type="checkbox"/> Nonpublication Request under 35 U.S.C. 122 (b)(2)(i). Applicant must attach form PTO/SB/35 or it's equivalent 17. <input type="checkbox"/> Other:	

18. If a CONTINUING APPLICATION, check appropriate box and supply the requisite information below and in a preliminary amendment, or in an Application Data Sheet under 37 CFR 1.76:

☒ Continuation ☐ Divisional ☐ Continuation-in-part (CIP) | of prior application No.: 09/804,690 filed March 12, 2001.

Prior application information: Examiner: Misook Yu Group Art Unit: 1642

For CONTINUATION OR DIVISIONAL APPS only: The entire disclosure of the prior application, from which an oath or declaration is supplied under Box 5b, is considered a part of the disclosure of the accompanying continuation or divisional application and is hereby incorporated by reference. The incorporation can only be relied upon when a portion has been inadvertently omitted from the submitted application parts.

### 19. CORRESPONDENCE ADDRESS

<input type="checkbox"/> Customer Number		Insert Customer No.		<input checked="" type="checkbox"/> Correspondence address below	
NAME	Bertram I. Rowland, Esq., Lumen Intellectual Property Services, Inc.				
ADDRESS	2345 Yale Street, 2 <sup>nd</sup> Floor				
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Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

NY2: 1476341.1

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Prior application:

Examiner Misook YuArt Unit 1642Conf. No. 1876

Commissioner for Patents

P.O. Box 1450

Mail Stop PATENT APPLICATION

Alexandria, VA 22313-1450

Sir:

This is a request for filing a ☒ continuation ☐ divisional application under 37 CFR § 1.53(b) of pending U.S. application no. 09/804,690 filed March 12, 2001

of Stanley COHEN and Limin LI

(inventor(s) currently of record in prior application)

for MAMMALIAN TUMOR SUSCEPTIBILITY GENES AND THEIR USES

(title of invention)

1. ☒ The filing fee is calculated below in view of the Preliminary Amendment referred to in paragraph 2 below:

## PATENT APPLICATION FEE VALUE

TYPE	NO. FILED	LESS	EXTRA	EXTRA RATE	FEE
Total Claims	8	- 20	0	\$18.00 each	\$ 0.00
Independent	3	- 3	0	\$86.00 each	\$ 0.00
Minimum Fee					\$ 770.00
Multiple Dependency Fee If Applicable (\$280.00)					\$ 290.00
<b>Total</b>					\$ 1060.00
Applicant qualifies for the 50% Reduction for Independent Inventor, Nonprofit Organization or Small Business Concern					\$ 530.00
<b>Total Filing Fee</b>					\$ 530.00

2. ☒ Claims 1-23 have been canceled, without prejudice, and new Claims 24-28 have been added as set forth in the Preliminary Amendment Under 37 C.F.R. § 1.115 filed on even date herewith.
3. ☒ Please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150. A copy of this sheet is enclosed.
4. ☒ The specification has been amended to update the cross reference to related applications as set forth in the Preliminary Amendment Under 37 C.F.R. § 1.115 filed on even date herewith.
5. ☒ Informal drawings are enclosed (one figure on one sheet).

6. ☒ The prior application is assigned of record to The Board of Trustees of the Leland Stanford Junior University.
7. ☒ A copy of the Power of Attorney filed in the prior application no. 09/804,690 filed March 12, 2001 is enclosed.
8. ☒ Additional enclosures or instruction: (a) Preliminary Amendment Under 37 C.F.R. § 1.115; and (b) Application Data Sheet Under 37 C.F.R. § 1.76.

Respectfully submitted,

By: *Stephen G. W.*, Reg. No. 43,171

Date: October 29, 2003

*Bertram I. Rowland* 20,015  
 Bertram I. Rowland (Reg. No.)  
 LUMEN INTELLECTUAL PROPERTY  
 SERVICES, INC.  
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 Palo Alto, California 94306  
 (650) 424-0100

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Prior application: Examiner Misook Yu  
 Art Unit 1642  
 Conf. No. 1876

Commissioner for Patents  
 P.O. Box 1450  
 Mail Stop PATENT APPLICATION  
 Alexandria, VA 22313-1450

Sir:

This is a request for filing a ☒ continuation ☐ divisional application under 37 CFR § 1.53(b) of pending U.S. application no. 09/804,690 filed March 12, 2001

of Stanley COHEN and Limin LI  
 (inventor(s) currently of record in prior application)

for MAMMALIAN TUMOR SUSCEPTIBILITY GENES AND THEIR USES  
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Respectfully submitted,

By: Stephen G. U., Reg. No. 43,171

Date: October 29, 2003

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Cohen et al.

Confirmation No.: To be assigned

Application No.: To be assigned; Continuation Art Unit: To be assigned  
of U.S. Application No. 09/804,690 filed  
March 12, 2001

Filed: On even date herewith

Examiner: To be assigned

For: MAMMALIAN TUMOR  
SUSCEPTIBILITY GENES AND  
THEIR USES

Attorney Docket No: S93-160 CON2

PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.115

Mail Stop PATENT APPLICATION  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Sir:

Pursuant to Rule 115 of the Rules of Practice, please enter the amendments set forth below and consider the remarks which follow. Applicants submit concurrently herewith: (a) a Request for Filing Continuation Application which includes a Patent Application Fee Value determination with provision for the appropriate fee; and (b) an Application Data Sheet Under 37 C.F.R. § 1.76.

AMENDMENTS TO THE SPECIFICATION begin on page 2 of this paper.

AMENDMENTS TO THE CLAIMS are reflected in the listing of the claims which begins on page 4 of this paper.

REMARKS begin on page 5 of this paper.

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph starting on page 1, line 1, with the following:

This application is a continuation of U.S. Patent Application No. 09/804,690, filed March 12, 2001, which is a continuation of application Ser. No. 09/146,187, filed September 1, 1998, now U.S. Patent No. 6,248,523, which is a division of application Ser. No. 08/977,818, filed Nov. 25, 1997, now U.S. Pat. No. 5,807,995, which is a division of application Ser. No. 08/670,274, filed Jun. 13, 1996, now U.S. Pat. No. 5,891,668, which is a continuation-in-part of application Ser. No. 08/585,758, filed Jan. 16, 1996, U.S. Pat. No. 5,679,523 which claims the benefit of U.S. provisional patent application No. 60/006,856, filed Nov. 16, 1995, the disclosures of which are herein incorporated by reference.

Please replace the paragraph starting on page 6, line 3, with the following:

The full length human cDNA contains an ~~1140~~ 1170 bp open reading frame, encoding a ~~380~~ 390 amino acid protein (GenBank Accession No. U82130). The human and mouse cDNAs are 86% identical at the nucleotide level. The predicted proteins are 94% identical and are distinguished by 20 amino acid mismatches and one gap. A coiled-coil domain (human TSG101 aa 231-302) and a proline-rich domain (human TSG101 aa 130-205, 32% proline) typical of the activation domains of transcription factors are highly conserved between the human and mouse proteins, with only one amino acid mismatch in each of the two domains. The leucine zipper motif in the coiled-coil domain of the human TSG101 protein is identical to the one in the mouse protein.

Please replace the paragraph starting on page 33, line 22, with the following:

A 1494 bp cloned human cDNA insert (which was deposited under the Budapest Treaty at the American Type Culture Collection, Manassas, VA 20110-2209 on June 17, 2003 with Accession No. PTA-5265) was termed full length TSG101 cDNA. Sequence analysis of this cDNA identified a 1140 bp open reading frame predicted to encode a 380 amino acid protein with a molecular mass of 42.841 kDa and a pI of 5.87. The human and mouse cDNAs are 86% identical at the nucleotide level. The predicted proteins are 94% identical and are distinguished by 20 amino acid mismatches and one gap. A coiled-coil domain (human TSG101 aa 231-302) and a proline-rich domain (human TSG101 aa 130-205, 32% proline) typical of the activation domains of transcription factors are highly conserved



between the human and mouse proteins, with only one amino acid mismatch in each of the two domains. The leucine zipper motif in the coiled-coil domain of the human TSG101 protein is identical to the one in the mouse protein. Other conserved features identified in human TSG101 include seven putative protein kinase C phosphorylation sites (aa 11, 38, 86, 89, 215, 225, 357), five potential casein kinase II phosphorylation sites (aa 38, 210, 249, 265, 290) and three potential N-glycosylation sites (aa 44, 150, 297). Analysis of the human TSG101 cDNA and protein sequences by the BLAST program search of NCBI database did not reveal any significant homology with the sequences for any other human genes.

Please replace the nucleic acid sequence of SEQ ID NO:3 with the following:

```

1  gaaggggtgtg  cgatttgtgtg  ggacgggtctg  gggcagccca  gcagcggctg  accctctgcc
61  tgcgggggaag  ggagtcgcca  ggcgcccgtc  atggcggtgt  cggagagcca  gctcaagaaa
121 atgggtgtcca  agtacaaata  cagagacctt  actgtacgtg  aaactgtcaa  tggtattact
181 ctatacaaaag  atctcaaacc  tgttttggat  tcatatgttt  ttaacgatgg  cagttccagg
241 gaactaatga  acctcactgg  aacaatccct  gtgccttata  gaggttaatac  atacaatatt
301 ccaatatgcc  tatggctact  ggacacatac  ccatataatc  cccctatctg  ttttgtttaag
361 cctactagtt  caatgactat  taaaacagga  aagcatgttg  atgcaaatgg  gaagatatat
421 cttccttata  tacatgaatg  gaaacaccca  cagtcagact  tgttggggct  tattcaggtc
481 atgatttgtg  tatttggaga  tgaacctcca  gtcttctctc  gtccattttc  ggcacccat
541 ccgccatacc  aggcaacggg  gccaccaaat  acttcctaca  tgccaggcat  gccagggtgga
601 atctctccat  acccatccgg  ataccctccc  aatcccagtg  gttaccagg  ctgtccttac
661 ccacctggtg  gtccatatcc  tgccacaaca  agttctcagt  acccttctca  gcctcctgtg
721 accactgttg  gtcccagtag  ggatggcaca  atcagcgagg  acaccatccg  agcctctctc
781 atctctgcgg  tcagtacaaa  actgagatgg  cggatgaagg  aggaaatgga  tcgtgccag
841 gcagagctca  atgccttgaa  acgaacagaa  gaagacctga  aaaaggggtca  ccagaaactg
901 gaagagatgg  ttaccggttt  agatcaagaa  gtagccgagg  ttgataaaaa  catagaactt
961 ttgaaaaaga  aggatgaaga  actcagttct  gctctggaaa  aaatggaaaa  tcagtctgaa
1021 aacaatgata  tcgatgaagt  tatcattccc  acagctccct  tatacaaaaca  gatcctgaat
1081 ctgtatgcag  aagaaaacgc  tattgaagac  actatctttt  acttggggaga  agccttgaga
1141 agggggcgtg  tagacctgga  tgtcttctct  aagcatgtac  gtcttctgtc  ccgtaaacag
1201 ttccagctga  gggcactaat  gcaaaaagca  agaaagactg  ccggtctcag  tgacctctac
1261 tgacttctct  gataccagct  ggaggttgag  ctcttcttaa  agtattcttc  tcttctttt
1321 atcagtaggt  gccagaata  agttattgca  gtttatcatt  caagtgtaaa  atattttgaa
1381 tcaataatat  attttctgtt  ttcttttggt  aaagactggc  ttttattaat  gcactttcta
1441 tcctctgtaa  actttttgtg  ctgaatgttg  ggactgctaa  ataaaatttg  tttt

```

Please replace the amino acid sequence of SEQ ID NO:4 with the following:

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MAVSESQLKQMVSKYKYRDLTVRETQNVITLYKDLKPVLDSYVFNDGSSRELMLNLGTIPVYPYRGNTYN
IPICLWLLDTPYNPPICFVKPTSSMTIKTGKHDANGKIYLPYLHEWKHPQSDLLGLIQVMIVVFGDEPPVFSR
PISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPPNPSGYPGCPYPPGPGYPATTSSQYPSQPPVTVGPSRDG
TISEDITRASLISAVSDKLWRMKEEMDRAQAELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKK
DEELSSALEKQENQSENNDIDEVLIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDFLKHVRLLSRK
QFQLRALMQKARKTAGLSLDLY

```

## AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

Claims 1-23 (Canceled).

24. (New) A substantially purified polypeptide comprising the full length human TSG101 protein encoded by a 1494 bp cloned human cDNA insert (SEQ ID NO:3).

25. (New) The purified polypeptide of claim 24, wherein said 1494 bp cloned human cDNA insert (SEQ ID NO:3) is deposited as ATCC Accession No. PTA-5265 in cloning vector pAMP1.

26. (New) A substantially purified polypeptide comprising the human TSG101 protein as described by the amino acid sequence of GenBank Accession No. U82130.

27. (New) A substantially purified polypeptide comprising the amino acid sequence of SEQ ID NO:4.

28. (New) A composition comprising a substantially purified polypeptide of any one of claims 24-27 in conjunction with a suitable pharmaceutical carrier.

### REMARKS

The subject application is a continuation of co-pending U.S. Patent Application No. 09/804,690 filed March 12, 2001. The specification has been amended hereinabove to include the appropriate priority information. The specification has also been amended to recite the GenBank Accession No. of the nucleic acid sequence and amino acid sequence of the TSG101 cDNA and protein. The specification has further been amended to recite the ATCC deposit accession number of the clone containing the TSG101 cDNA. Finally, the specification has been amended with substitute sequences for SEQ ID NO:3 and SEQ ID NO:4.

Claims 1-23 have been canceled without prejudice, and new claims 24-28 have been added. Support for new claims 24-25 is found in the specification at page 15, lines 7-9; page 33, lines 22-23; page 34, line 13-18; and page 40, lines 3-6. Support for new claim 26 is found in the specification at page 6, lines 3-4; and page 15, lines 7-9. Support for new claim 27 is found in the specification at page 7, lines 7-8; and page 15, lines 7-9. Support for new claim 28 is found in the specification at page 22, lines 19-27. Upon entry of the above-made amendments, claims 24-28 will be pending.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the foregoing remarks are respectfully requested.

Respectfully submitted,

*Bj. Stephen K. Sullivan, Reg. No. 43,171*

Date: October 29, 2003

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